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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/750,878	01/05/2004	Hans-Michael Eggenweiler	MERCK-2412-D01	3232

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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 01/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/750,878	EGGENWEILER ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 5-9 is/are pending in the application.

4a) Of the above claim(s) 9 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 5-8 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed October 14, 2005 have been entered. The addition of claim 9 is acknowledged.

Claims 5-9 are pending.

Claim 9 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected specie, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on April 2, 2005.

The outstanding rejection under 35 USC 112, second paragraph is withdrawn in view of the amendments filed October 24, 2005.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not provide sufficient information that all tumors are treatable by the herein claimed compounds described in the methods claimed.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) **The nature of the invention**

All of the rejected claims are drawn to an invention which pertains to a method of treating mammals with variously substituted benzopyrano-imidazole compounds for the inhibition of tumor growth. The nature of the invention is complex in that it encompasses the treatment of all types of tumors.

(2) **Breadth of the Claims**

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass inhibition of any number of tumors by the herein claimed benzopyrano-imidazole compounds.

(3) **Guidance given by the instant specification**

The guidance given by the specification as to how one would administer the herein claimed compounds to a subject in order to inhibit any type of tumor growth is

limited. All of the guidance provided by the specification is directed toward the possibilities of treating tumor by PDE IV inhibitors (See the instant specification, page 3, lines 30-33). The instant specification does not mention of how PDE VII be able to be used as anti-tumor agents. Examiner notes that "the instant specification states that PDE VII inhibitors may also inhibit the growth of tumor cells" [emphasis added].

(4) **Working Examples**

There is no working example disclosed in the instant specification.

(5) **State of the Art**

While the state of the art is relatively high with regard to treating specific cancers or tumors, the state of the art with regard to treating cancer or tumor generally is underdeveloped. In particular, there is no known anticancer agent which is effective against all cancers. Carter et al. (Chemotherapy of Cancer 2nd ed 1981) clearly teaches that for the forty known anticancer agents, none are effective against all cancers (pages 362-365). There are compounds that treat a range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-I), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Even those that affect a single organ are often not generally

treatable. For example, the main types of lung cancer are small cell (oat cell), giant cell, clear cell, adenocarcinoma of the lung, squamous cell cancer of the lung, and mesothelioma. There is no such thing as a treatment of these generally because of their diversity. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.

(6) **Predictability of the Art**

The invention is directed to inhibiting tumor growth in general. It is well established that "the scope of enablement various inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839 (1970). Cancers are especially unpredictable due to their complex nature. Please refer to the discussion of Carter, et al. and the state of the art in (5) that shows the different treatments of cancers. The treatment of one type of cancer or tumor could not be necessarily the same for the other type.

(7) **The Quantity of Experimentation necessary**

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of an appropriate pharmaceutical carrier, a dosage for each compound, the duration of treatment, route of treatment, etc. and, in the case of human treatment, an appropriate animal model system for one of the claimed compounds. One would then need to test the combination in the model system to determine whether or not the combination is effective for inhibiting cancer cells. If unsuccessful, which is likely

given the lack of significant guidance from the specification or prior art regarding treatment of cancer with any herein claimed compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. If again unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding treatment of cancer with any compound, the entire, unpredictable process would have to be repeated until successful. In order to practice Applicant's invention, it would be necessary for one to conduct the preceding experimentation for each type of cancer because, as described by Carter, et al., there is no known drug effective for inhibiting all types of cancer. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to inhibit cancer cells in a mammal by administration of one of the compounds within the claims.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, a method for inhibiting tumor growth generally by administering the herein claimed various benzopyrano-imidazole compounds is not considered to be enabled by the instant specification.

Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for rheumatoid arthritis, multiple sclerosis, Crohn's disease, diabetes mellitus, and ulcerative colitis, does not reasonably provide enablement for other autoimmune disorders. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In the instant case, the specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) **The nature of the invention**

All of the rejected claims are drawn to an invention which pertains to a method of treating mammals with variously substituted benzopyrano-imidazole compounds for the treatment of autoimmune disorders. The nature of the invention is complex in that it encompasses the treatment of all types of autoimmune disorders.

(2) **Breadth of the Claims**

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass inhibition of any number of autoimmune disorders, whether they are mediated by TNF-α or not, by the herein claimed benzopyrano-imidazole compounds.

(3) **Guidance given by the instant specification**

The guidance given by the specification as to how one would administer the herein claimed compounds to a subject in order to inhibit any type of autoimmune disorders is limited. All of the guidance provided by the specification is directed toward the possibilities of treating autoimmune disorders by PDE VII inhibitors because of its TNF-α inhibitory effect (See the instant specification, page 3, lines 8-15).

(4) **Working Examples**

There is no working example disclosed in the instant specification.

(5) **State of the Art**

While it is known that some drugs are useful for treating multiple autoimmune diseases, other drugs are not as versatile. Christodoulos et al. teaches that minocycline can be used to treat rheumatoid arthritis, but can also lead to drug-induced lupus, another autoimmune disease for example (Chest. 1999;115(5): 1471).

(6) **Predictability of the Art**

Multiple claims are directed to treatment of autoimmune conditions in general. It is well established the "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiology activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833,839 (1970. The art is

unpredictable because the treatment of one type of autoimmune condition will not necessarily be the same for the other type.

(7) **The Quantity of Experimentation necessary**

In order to practice the claimed invention, one of skill in the ad would have to first envision a combination of an appropriate pharmaceutical carrier, a dosage for each compound, the duration of treatment, route of treatment, etc. and, in the case of human treatment, an appropriate animal model system for one of the claimed compounds. One would then need to test the combination in the model system to determine whether or not the combination is effective for decreasing the amount of therapeutic agent needed to treat an autoimmune disease. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding sparing the amount of therapeutic agent administered to a. patient with an autoimmune disease by administering a sleep restorative agent, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compounds, compound dosage, duration of treatment, route of administration, etc. and appropriate model system, or envision an entirely new combination of the above and test the system again. If again unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding the treatment of an autoimmune disease, the entire, unpredictable process would have to be repeated until successful. In order to practice Applicant's invention, it would be necessary for one to conduct the preceding experimentation for each type of autoimmune disease because, as shown by Christodoulos et al., some drugs will not necessarily treat all types of autoimmune

conditions. Therefore, it would require undue experimentation to practice the claimed invention of decreasing the effective amount of a recited therapeutic agent administered to a subject having an autoimmune condition by administering the benzopyrano-imidazole agent recited in the claims.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, a method for inhibiting tumor growth generally by administering the herein claimed various benzopyrano-imidazole compounds is not considered to be enabled by the instant specification.

Claims 5-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not provide sufficient information that memory disturbances are treatable by the herein claimed compounds described in the methods claimed.

The specification does not provide sufficient information that all tumors are treatable by the herein claimed compounds described in the methods claimed.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is

directed to *In re Wands*, 8USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) **The nature of the invention**

All of the rejected claims are drawn to an invention which pertains to a method of treating mammals with variously substituted benzopyrano-imidazole compounds for the treatment of memory disturbances. The nature of the invention is complex in that it encompasses the treatment of all types of memory disturbances.

(2) **Breadth of the Claims**

The claims are so broad that they encompass any mental status changing disorder that could potentially affect CNS.

(3) **Guidance given by the instant specification**

There is no guidance as to how PDE VII inhibitors related to memory disturbances. No guidance as o how to treat such disorders is disclosed.

(4) **Working Examples**

There is no working example disclosed in the instant specification.

(5) **State of the Art**

It is known in the art the herein claimed benzopyrano-imidazole compounds as CNS depressants (See the abstract of Savel'ev et al. Khimiko-Farmatsevticheskii Zhurnal, 1993;17(6):697-700), which is a sedative agent. Sedative agent will generally cause memory disturbances rather than treating the same.

(6) **Predictability of the Art**

Multiple claims are directed to treatment of autoimmune conditions in general. It is well established the "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiology activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833,839 (1970).

(7) **The Quantity of Experimentation necessary**

In order to practice the claimed invention, one of skill in the art would have to first envision the use of a sedative agent, which is commonly causing memory disturbance, to treat memory disturbance. There is no guidance in the instant specification to the one of skilled in the art as to how to go by employing a contradictory effect for treatment.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, a method for inhibiting tumor growth generally by administering the herein claimed various benzopyrano-imidazole compounds is not considered to be enabled by the instant specification.

Response to Arguments

Applicant's arguments filed October 24, 2005 averring the office's failure to provide evidence pointing out the reason why the compounds are not enabled for the herein claimed invention have been considered, but are not found persuasive. Examiner notes that it is very clear in the previous office action evidences have been provided in Carter casting doubts on the truth of what is claimed that no known single magic bullet is effective for treating all of the tumors. Furthermore, the instant specification does not even provide any guidance as to PDE VII inhibition in relation to the treatment of tumor growth and/or metastasis. Therefore, even considered the skill of skilled artisan possesses, the instant specification still not providing sufficient information as to how to practice the full scope of the claims. In order to determine whether the instant claims are enabled for its full scope, the Examiner had discussed the eight factors clearly in the previous office action. In view of the discussion with provided evidence, the skilled artisan would have to perform undue experimentation to find out what is working and what is not as to the treatment of tumor growth and metastasis. Therefore, the instant claims are considered to be properly rejected under 35 USC 112, first paragraph.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Primary Examiner
Art Unit 1617